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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/506,079	02/16/2000	Gail M. Clinton	49321-16	5713

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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
09/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/506,079	CLINTON ET AL.	
	Examiner	Art Unit	
	ANNE L. HOLLERAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,8-10,18-20 and 38-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *8,9,38,39 and 45-49* is/are allowed.

6)☒ Claim(s) *1,2,18-20 42 and 43* is/are rejected.

7)☒ Claim(s) *3, 10, 19, 20, 40, 41 and 44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/27/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/9/2008 has been entered.

The amendment filed 6/9/2008 is acknowledged.

Claims 1-3, 8-10, 18-20 and 38-49 are pending and examined on the merits.

Objections and Rejections Withdrawn:

The objection to claims 1, 8-10, 18, 38, and 39 for typographical errors is withdrawn in view of the amendment to the claims.

New Grounds:

Claim Objections

Claims 3, 10, 19, 20, 40, and 41 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 is broader in scope than

claim 1, from which it depends. Claim 1 recites the polypeptides with specifically indicated residues for SEQ ID NOS: 19-28, whereas claim 3 recites polypeptides that are SEQ ID NOS: 19-28, and therefore includes subject matter that is broader than that of claim 1. Claim 10 is broader in scope than claim 8, from which it depends. Claim 8 recites the polypeptides with specifically indicated residues for SEQ ID NOS: 29-38, whereas claim 10 recites polypeptides that are SEQ ID NOS: 29-38, and therefore includes subject matter that is broader than that of claim 8. Claims 19, 20, 40 and 41 are broader in scope than independent claim 18, from which claims 19, 20, 40 and 41 depend. Claim 18 recites fragments that comprise specific residues *and* are about 50-79 contiguous residues in length, or fragments that comprise specific residues *and* are about 80-419 continuous residues in length *and* wherein the C terminal 79 contiguous amino acids are present. In contrast, claims 19, 20, 40 and 41 recite fragments of about 50-79 contiguous residues in length, or 80-419 contiguous amino acids in length, which is broader in scope than the fragments recited in claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 19 and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Doherty-II (U.S. 6,414,130; published Jul. 2, 2002; effective filing date Jan. 20, 1999; of record).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 19 and 20 do not receive benefit of priority to the parent application, 09/234,208, because SEQ ID NOS: 14, and 19-28 are not found in the parent application. Therefore, the filing date of the instant application is used for comparison with the prior art (2/16/2000).

Claims 19 and 20, which include subject matter outside the scope of claim 18, from which these claims depend, are drawn to pharmaceutical compositions comprising an agent that is an isolated polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NOS: 14 and 19-28, and fragments thereof of about 50 to 79 contiguous residues in length, and in the case of claim 20, the pharmaceutical composition further comprises a monoclonal antibody that binds to the extracellular domain of Her-2.

Doherty discloses SEQ ID NO: 1 and SEQ ID NO: 2, which are the amino acid sequences of Herstatin and its C-terminal 79 amino acid fragment. The claims are drawn to pharmaceutical compositions comprising polyeptides that comprise a sequence as small as 50 contiguous amino acids taken from SEQ ID NOS: 19-28. Fragments as small as 50 amino acids in length will have 100 percent identity with fragments of Doherty's SEQ ID NO: 1. Therefore,

a polypeptide comprising a subsequence of 50 amino acids in length from, for example SEQ ID NO: 19, will be a polypeptide that has the same sequence as the sequences of SEQ ID NO: 1 or SEQ ID NO: 2 of Doherty-II. Doherty-II teaches pharmaceutical compositions comprising such polypeptides, and also comprising a monoclonal antibody that binds to the extracellular domain of Her-2. Therefore, Doherty-II teaches the pharmaceutical compositions as claimed.

Claim Rejections Maintained:

Claims 1, 2, 18, 42 and 43 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the amendment filed 9/24/2007 introduces new matter into the specification as originally filed.

Applicant's arguments have been carefully considered, but fail to persuade. Applicant argues that even if one implies a negative limitation or proviso clause as urged by the examiner, there is no requirement under US patent law to have a "literal basis" for such negative limitation or proviso clause; There is not requirement that the specification have "literal support" for a limitation that the fragments must comprise the residues that are different from the previously disclosed Herstatin. Applicant cites In re Johnson 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA1977) and the MPEP 2173.05(i) as a basis for the statement that applicant is entitiled to "carve out" a portion of the disclosed subject matter, whether it be done by merely claiming a portion of the invention, or through a negative limitation or proviso clause.

In response, the examiner notes that in the previous rejection the MPEP2173.05(i) was not characterized by the examiner as supporting a requirement for "literal support", merely that any negative limitation or exclusionary proviso must have basis in the original disclosure. Originally filed claim 1 was drawn to: "An isolated polypeptide having from about 50-79 amino acids taken from the sequence of SEQ ID NO: 1, wherein the polypeptide binds to the extracellular domain ECD of Her-2 at an affinity of at least 10^{8}". SEQ ID NO: 1 is an amino acid sequence, 79 amino acids in length, with the following residues defined as: position 2 is Thr or Ser, position 5 is Leu and Pro, position 6 is Pro or Leu, position 16 is Leu or Gln, position 18 is Met or Leu, position 21 is Gly, Asp, Ala or Val, position 36 is Leu or Ile, position 54 is Pro or Arg, position 64 is Pro or Leu, position 73 is Asp or Asn. The specification provides Table 1, describing 11 splice variants, one of which (variant 11) is the subject of US Patent application 09/234,208, now US Patent 7,393,823. Additionally, the specification provided Figure 8, which has a sequence that is within the scope of SEQ ID NO: 1. The disclosure of SEQ ID NO: 1 is broader in scope than what is provided by the disclosure of Table 1 and Figure 8, because SEQ ID NO: 1 allows for sequences not found in Table 1 and Figure 8. Applicant then amended the disclosure of the specification by submitting a new sequence listing that separated out individual sequences that corresponded to those found in Table 1 (excluding variant 11) and Figure 8 (SEQ ID NOS: 14 and 19-28).

Applicant has now amended the claim 1 by adding the limitation: "and wherein the polypeptide comprises: with respect to SEQ ID NO: 14, at least one of the position 6 Pro and the position 73Asp; with respect to SEQ ID NO: 19, the position 2 Ser; with respect to SEQ ID NO: 20, the position5 Pro; with respect to SEQ ID NO: 21, both the position 6 Leu and position 73

Asp; with respect to SEQ ID NO: 22, the position 16 Gln; with respect to SEQ ID NO: 23, the position 18 Leu; with respect ot SEQ ID NO: 24, the position 21 Asp, Ala or Val; with respect to SEQ ID NO: 25, the position 36 Ile; with respect to SEQ ID NO: 26, the position 54 Arg; with respect to SEQ ID NO: 27, the position 64 Leu; or with respect to SEQ ID NO: 28, both the position 6 Pro and the position 73 Asn.

Applicant states that the new limitation has support in the original disclosure because the ECDIIIa variant containing polypetpides, both comprising the ECDIIIa or sub fragments thereof are indeed encompassed within the original specification teachings. The independent claims have merely been amended to delineate the variant residues, including subfragment residues. Applicant states that support for this amendment is explicitly found in Table 1 on page 33 of the originally filed specification (see also, for example, original claim 27 reciting "ECDIIa variant sequence). Additionally, applicant points to the specification: "[t]his result demonstrates that in the human population there are several variations in the intron-8 encoded domain that could lead to altered biochemical and biological properties among ECDIIIa-containing variants" (page 32, lines 21-33). Applicant also points to this passage of the specification at page 14, lines 6-8 "[f]or the production of antibodies, various host animals may be immunized with e.g., polyhistidine-tagged ECDIIIa variants or mutants of the ECDIIIa region." Applicant points to this passage of the specification: "PCR, or reverse transcription can be utilized to identify nucleotide variation within the ECDIIIa domain" (page 17, lines 19-2"). Applicant also discusses a declaration made by Dr. Gail Clinton (of record; page 5,paragraph 5, of Declaration of Dr. Gail Clinton 19 April 2003, of record in this case). '[t]he discovery of these novel polymorphisms was precisely the reason that the present application was filed. The Herstatin sequence of the earlier U.S. patent

application (09/234,208) was already disclosed and claimed in that application, and it was the primary purpose of the present application to claim additional polymorphisms, while not claiming the previously claimed Herstatin. In Example 11 of the present application, the 1999 Doherty et al, PNAS paper (which lists the previously claimed Herstatin) was cited in the introduction. Example 11 then goes on to describe the additional, different polymorphisms by their nucleotide and deduced amino acid sequence. These additional variations in the intron-8 encoded domain were discovered in the human population and Table 1 sets forth those variants, including originally identified variant 11."

Applicant's arguments are not persuasive. First, applicant states that the independent claims have merely been amended to delineate the variant residues, including the subfragment residues. This appears to be a mischaracterization of the effect of the amendment presented in the paper filed 9/24/2007. The effect of the amendment is to specify what specific residues are encompassed by fragments for a given sequence. For example, with respect to SEQ ID NO: 14, before the amendment of 9/24/2007 (and that of 12/14/2006), claim 1 was drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 14 or fragments thereof of about 50 to 70 contiguous residues in length (i.e. any fragment within this length range), wherein the polypeptide binds to the extracellular domain (ECD) of Her-2 with an affinity binding constant of at least 10^8 M^{-1}. Now, with the current amendment, any fragment of 50 to 70 contiguous residues of SEQ ID NO: 14 must comprise at least one of position 6 Pro and the position 73 Asp. This amendment does not appear to "merely" delineate the variant residues, but instead changes the scope of the genus of fragments of SEQ ID NO: 14 of about 50 to 79 contiguous residues in length. Applicant goes on to say that support is "explicitly" found in

Table 1, on page 33. There is no "explicit" support for defining a genus of fragments in the manner set forth in the instant claims. Table 1 provides the sequence information for the variants of ECDIII polypeptides, but does not describe the genus of fragments of 50 to 79 amino acids in length, nor does it describe the subset of fragments of about 50 to 79 amino acids in length that must comprise the positions as set forth in the claims. Therefore, the examiner does not understand how the teachings of Table 1 are "explicit" support for the newly defined genus of fragments set forth in the present claims. Applicant then goes on to refer to passages in the specification that contemplate methods of making antibodies using variants or mutants of the ECDIIIa region. This teaching does not appear to have any relevance to the question of whether the specification provides support for the newly added limitations present in claim 1, because it appears to be referring to use of the entire ECDIIIa region. Finally applicant refers to a declaration filed by Dr. Gail Clinton (one of the named inventors of the present application), in which Dr. Clinton states that the purpose of filing the present application was to claim additional polymorphisms of Herstatin, which was the subject of the CIP parent of this application. The examiner does not dispute the statements of the Clinton declaration, but reminds applicant that support for any claim limitations must be found in the specification and the claims as originally filed.

Applicant also discusses case law, in particular *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA1977) to support the contention that there is nothing in US patent law that prohibits an applicant to "carve out" a patentable portion of what is disclosed in the specification. The discussion of *In re Johnson* by applicant appears to be for the purpose of supporting the assertion that applicant may claim less than the full scope of what was originally claimed.

However, the situation presented by the present application appears to be distinguished from the circumstances presented in *Johnson*. The new limitation that has been added to the claims in the present case is not analogous to the specific negative proviso at issue in *Johnson*, because in Johnson, specifically named species were excluded, whereas in the claims of the present application, a subgenus is excluded to make a new genus. Applicant's attention is drawn to *Purdue Pharma L.P. v. Faulding Inc.*, 56 USPQ2d 1481 (Fed. Cir. 2000), where applicant was prohibited from carving out a patentable portion of what is disclosed in their specification. Applicant's attention is drawn to *In re Welstead*, 174 USPQ 449 (CCPA 1972)) in which a new matter rejection was affirmed, where the alleged new matter was due to applicant's claiming less than what was originally claimed. Applicant cites but does not discuss in detail *In re Wertheim*, 191 USPQ 90, 97 (CCPA, 1976) and *In re Saunders* 170 USPQ 213, 220 (1971). These cases appear also to present situations that are distinguished from the situation in the present case. With respect to *Wertheim*, which concerned the question of whether claiming a smaller range within an originally claimed larger range presented new matter. In this case the court found that the subsumed range was part of applicant's disclosure because the range was smaller and there were two specific embodiments of 36% and 50% that were also within the claimed range. In the present case, the specification as originally filed does not provide any examples of fragments that may be used as guideposts for determining the boundary of the newly set forth genus of fragments. With respect to *Saunders*, this case does not appear to concern a new matter issue.

Applicant's arguments are unpersuasive and the rejection is maintained for the reasons of record.

Claims 3, 8-10, 38, 39, 44, 46-48 are not included in this rejection because the claims are either drawn to a polypeptide comprising the entire sequence of any of SEQ ID NOS: 14 and 19-28, or the claims are drawn to fragments of a larger sequence where the fragments inherently include all of any one of SEQ ID NOS: 14 and 19-28 as the C-terminal 79 contiguous amino acids. For example, the sequence of the C-terminal 79 contiguous amino acids of SEQ ID NO: 15 is the same as the sequence of SEQ ID NO: 14. In claim 8, which recites that the fragments are of about 80 to 419 contiguous residues in length, wherein the C-terminal 79 contiguous amino acids are present, the entire sequence of any one of SEQ ID NOS: 14 and 19-28 is included within each of the claimed polypeptides.

Conclusion

Claims 1, 2, 18-20, 42 and 43 are rejected. Claim 44 is objected to for depending from rejected claims, and claims 3, 10, 19, 20, 40 and 41 are objected to for failing to further limit a claim from which they depend. Claims 8, 9, 38, 39 and 45-49 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
September 5, 2008
/Alana M. Harris, Ph.D./

Primary Examiner, Art Unit 1643